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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/473,551	12/28/1999	Jeffrey D. Milbradt	6029-9879	1110

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EXAMINER	
CHERNYSHEV, OLGA N	
ART UNIT	PAPER NUMBER

1646  
DATE MAILED: 04/28/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	Application No.	Applicant(s)
	09/473,551	MILBRANDT ET AL.
	Examiner	Art Unit
	Olga N. Chernyshev	1646

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1) Responsive to communication(s) filed on 17 October 2002.

2a) This action is **FINAL**.                            2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4) Claim(s) 1 and 5-9 is/are pending in the application.

4a) Of the above claim(s) 5 is/are withdrawn from consideration.

5) Claim(s) \_\_\_\_\_ is/are allowed.

6) Claim(s) 1 and 6-9 is/are rejected.

7) Claim(s) \_\_\_\_\_ is/are objected to.

8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) The proposed drawing correction filed on \_\_\_\_\_ is: a) approved b) disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) All    b) Some \* c) None of:

1. Certified copies of the priority documents have been received.

2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.

3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) The translation of the foreign language provisional application has been received.

15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) Notice of References Cited (PTO-892)                            4) Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_.

2) Notice of Draftsperson's Patent Drawing Review (PTO-948)                    5) Notice of Informal Patent Application (PTO-152)

3) Information Disclosure Statement(s) (PTO-1449) Paper No(s) 33, 16                    6) Other: \_\_\_\_\_.

## **DETAILED ACTION**

### ***Continued Examination Under 37 CFR 1.114***

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on October 17, 2002 has been entered.

### ***Status of the claims***

2. Applicant is advised that because no request for entry of the amendment proposed in Paper No. 25, filed on June 10, 2002, was made by Applicant, the status of the pending claims remains as follows.

Claims 1 and 5-9 are pending in the instant application.

Claim 5 has been withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention by original presentation, there being no allowable generic or linking claim, see section 2 of paper No. 21.

Claims 1 and 6-9, in so far as they are directed to the elected chimeric peptides of SEQ ID NO: 23 and SEQ ID NO: 26 are under examination in the instant office action.

3. The Text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

4. Any objection or rejection of record, which is not expressly repeated in this action has been overcome by Applicant's response and withdrawn.

5. Applicant's arguments filed on October 17, 2002 have been fully considered but they are not deemed to be persuasive for the reasons set forth below.
6. The Declaration of J.D. Milbrandt under 37 CFR 1.132 filed October 17, 2002 is sufficient to overcome the rejection of claims 7 and 8 based upon lack of enablement.

***Claim Rejections - 35 USC § 112***

7. Claims 1, 6 and 9 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention for the reasons explained in section 4 of Paper No. 13 and section 6 of Paper No. 21.

Claims 1, 6 and 9 are directed to a polypeptide, which activates GFR $\alpha$ 1-RET but does not substantially activate GFR $\alpha$ 2-RET or GFR $\alpha$ 3-RET. The claims broadly describe the polypeptide as comprising a substituted persephin having different amino acids in the F2a and/or F2c regions, wherein the substitutions comprise from one to eight amino acids that are either identical to region F2a of a GDNF family ligand, or contain conservative amino acid substitutions of region F2a of a GDNF family ligand (see claim 1 and also page 6, first paragraph of the instant specification). However, the instant specification fails to provide enough guidance for one skilled in the art how to make a polypeptide encompassed by these claims. One skilled in the art readily understands that the claims, as written, encompass a vast number of polypeptides, including sequences where only one amino acid in F2a region is identical to region F2a of a GDNF family ligand, as well as sequences where all the amino acids of region F2a of a GDNF family ligand are represented by conservative substitutions. For reasons explained earlier in the previous

communications, the instant specification is found to be not enabling for this breadth of the claimed subject matter. Briefly, it is well known in the art that changing even one amino acid in a protein sequence leads to a new protein by definition and that amino acid structure cannot necessarily predict the function of the protein. The instant specification fails to teach how to make a polypeptide that would satisfy the broad structural limitations presented in the instant claims, which would activate GFR $\alpha$ 1-RET but does not substantially activate GFR $\alpha$ 2-RET or GFR $\alpha$ 3-RET. There are no working examples of single amino acid substitution, or disclosure of the minimal distinguishable structural features that lead to the desired function that would satisfy a skilled artisan and provide adequate enablement for practicing the claimed invention commensurate with the scope of these claims. In the absence of this crucial information, one skilled in the art would have to resort to substantial amount of undue experimentation to discover how to make and use the claimed polypeptide.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 1 and 6-9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

9. Claim 1 is vague and ambiguous for recitation of a polypeptide, which "comprises a persephin as set forth in SEQ ID NO: 1" and "further comprises substitutions in region F2a and substitutions in region F2c". The metes and bounds of the claimed subject matter cannot be determined from the claim because these two recitations appears to be mutually exclusive. The

claimed polypeptide either comprises SEQ ID NO: 1 or lacks it due to the substitutions on certain regions. It is not clear how a polypeptide can have a defined sequence structure and further lack it. Clarification is required.

10. Claim 6 is similarly vague and indefinite for the reasons as applied to claim 1 earlier. The claim recites the persephin of SEQ ID NO: 1 with certain substitutions, which appear to alter the structure of SEQ ID NO: 1, thus making the claimed subject matter ambiguous.

11. Claims 7-9 are indefinite for being dependent from indefinite claims.

*Allowable Subject Matter*

12. Claims 7 and 8 would be allowable if rewritten to overcome the rejection(s) under 35 U.S.C. 112, second paragraph, set forth in this Office action and to include all of the limitations of the base claim and any intervening claims.

*Conclusion*

13. No claim is allowed.

14. This application contains claim 5 drawn to an invention nonelected by original presentation in Paper No. 21. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Olga N. Chernyshev whose telephone number is (703) 305-1003. The examiner can normally be reached on Monday to Friday 9 AM to 5 PM ET.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on (703) 308-6564. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 782-9306 for regular communications and (703) 782-9307 for After Final communications.

Certain papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax center located in Crystal Mall 1 (CM1). The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers.

Official papers filed by fax should be directed to (703) 308-4556 or (703) 308-4242. If either of these numbers is out of service, please call the Group receptionist for an alternative number. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294. Official papers should NOT be faxed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Olga N. Chernyshev, Ph.D. *OC*  
April 25, 2003

  
JOHN ULM  
PRIMARY EXAMINER  
GROUP 1600